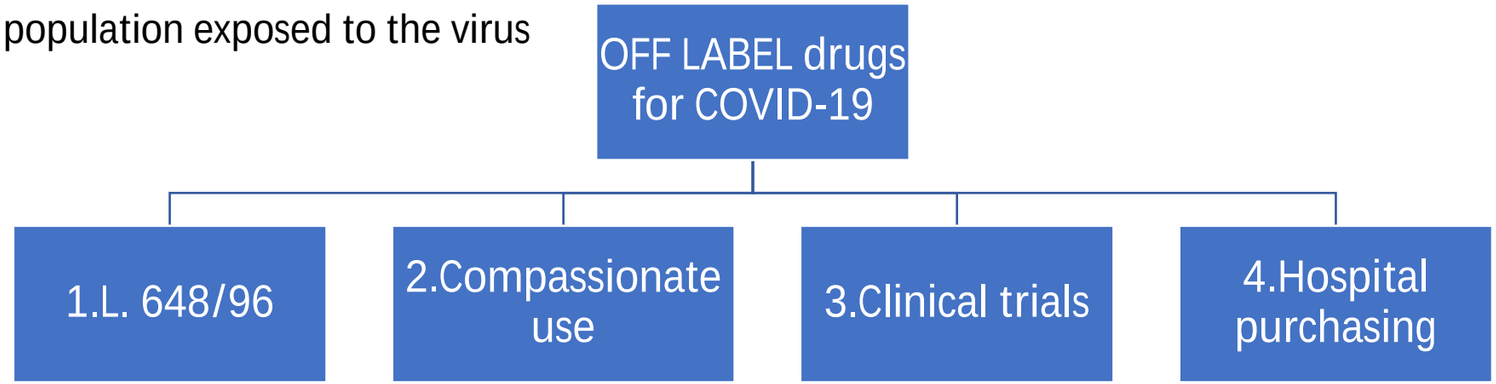
ITALIAN COMPETENT AUTHORITY STRATEGY COVID 19 PANDEMIC EMERGENCY

COVID - 19

The Italian Medicines Agency has taken some timely actions to encourage early access and facilitate the conduct of clinical studies on the efficacy and safety of new therapies used for the treatment of COVID-19 disease:

- Continuous information on medicines
- Recommendations on the use of drugs in the population exposed to the virus
- Use of drugs under special circumstances
- Clinical trials and access to new drugs



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1. OFF LABEL USE – LAW 648/96

COVID - 19

The AIFA Technical Scientific Committee has expressed a favorable opinion on the inclusion (law 648/96) of the off label use of the following medicines for the treatment of SARS-CoV-2 infection:

1. **hydroxychloroquine (Plaquenil®):** antimalarial drug (antiparasitic and antirheumatic) belonging to the 4-aminoquinolinics family, with preliminary data of potential antiviral activity - **Hydroxychloroquine**
2. **lopinavir / ritonavir (Kaletra®):** antiviral agents for the treatment of HIV infection: lopinavir leads to protease inhibition boosted with ritonavir - **Lopinavir / ritonavir**
3. **darunavir / cobicistat (Rezolsta®):** antiviral agents for the treatment of HIV infection: darunavir is an inhibitor of HIV protease 1 and cobicistat is a selective inhibitor of cytochrome - **Darunavir / cobicistat**
4. **Low-molecular-weight heparin (LMWH):** class of anticoagulant medications, glycosaminoglycans obtained by heparin - **Low-molecular-weight heparin (LMWH)**
5. **Azithromycin:** antibiotic of azalide class, a type of macrolide antibiotic - **Azithromycin**

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Off Label Use – Law 648/96

Intentional therapeutic use of a medicinal product for an indication not included in the SmPC of the authorised product

Inclusion is evaluated by AIFA upon documented request by Patient Associations, Scientific Societies, Clinicians, or on AIFA CTS request.

Documentation needed:

- Scientific report on the pathology that represents its severity and the absence of a valid therapeutic alternative;
- Rationale, scientific publications and clinical data (phase I and II studies) to support the proposed treatment;
- Description of the proposed therapeutic plan;
- Estimate of the number of patients who could benefit from the treatment on the national territory;
- Cost estimate for the proposed treatment;
- Information concerning ongoing clinical trials;
- The authorization status of the medicinal product in Italy and abroad

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2. COMPASSIONATE USE (D.M.07/09/17)

COVID - 19

All the approved treatments will be published on the institutional website of AIFA (section "Emergency COVID-19"), and the current approved therapy under compassionate use is:

- **Ruxolitinib:** antineoplastic agent, selective inhibitor of Janus Associated Kinases (JAK1 and JAK2). Indication: for patients diagnosed with COVID19 and severe/very severe lung disease - Ruxolitinib
- **Canakinumab:** human monoclonal antibody anti-interleukin-1 beta. Indication: treatment of cytokine release syndrome (CRS) in patients with COVID-19-induced pneumonia - Canakinumab
- **Remdesivir:** antiviral agent, nucleotide analogue, treatment for Ebola virus disease and Marburg virus infections. Indication: treatment of SARS-CoV2 (CoV) Infection - Remdesivir

As indicated, the request to start compassionate use programs for the treatment of COVID-19 must be sent in advance to the Single National Ethics Committee identified by the law (INMI L. Spallanzani) and to AIFA.
The opinion of the Single National Ethics Committee is expressed with an emergency procedure and it is immediately applicable for all the centers and all the patients treated, while the **nominal therapeutic uses** remain under responsibility of the local ethics committees.

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Compassionate use (D.M.07/09/17)
treatment option that allows the use of an unauthorized medicine. Under strict conditions, products in development can be made available to groups of patients who have a disease with no satisfactory authorised therapies and who cannot enter clinical trials.

Inclusion is evaluated by AIFA and by the Single Ethic Committee upon documented request by Clinicians.

Documentation needed:

- Letter of transmission to AIFA and National Ethics Committee of INMI Spallanzani (cover letter)
- EudraCT number
- OsSC Application Form (Appendix 5
- Possible delegation of the Promoter to the CRO
- Study protocol
- Synopsis of the study
- Patient information documentation and informed consent form
- CV and declaration of conflict of interest of the Principal Investigator
- Investigator Brochure (IB) if available
- Investigational Medicinal Product Dossier (IMPD) or Summary of theProduct Characteristics (SmPC)
- GMP production/import
- Experimental medicinal product label

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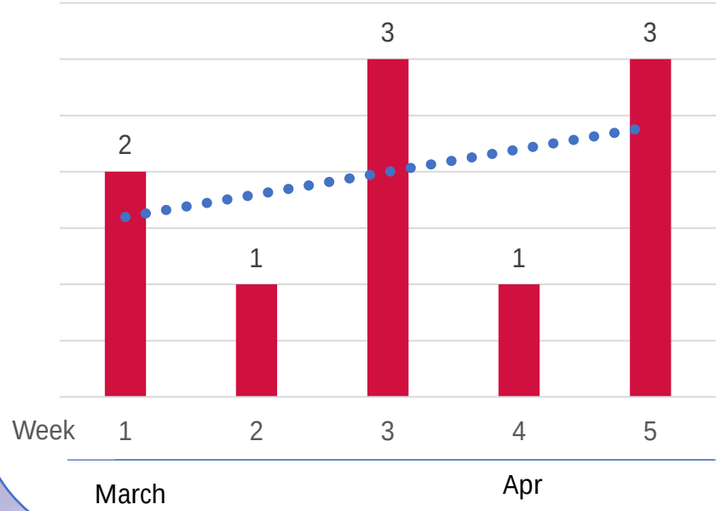
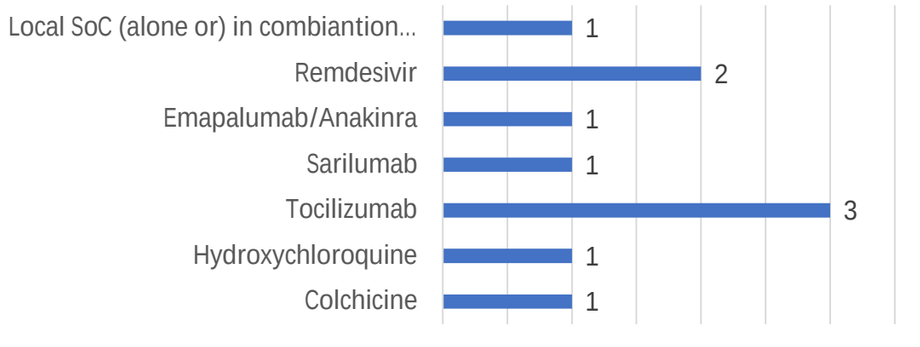
3. CLINICAL TRIALS

COVID - 19

AIFA has been involved with the task of evaluating all clinical trials on drugs for patients with COVID-19 (Italian Healthcare Decree Law Art. 17).
Updated information on ongoing trials and related documents has been reported in the AIFA web site (link below) with all the trials already authorized (date of authorization, name of the trial and of the investigational drug, Sponsor).



TOTAL CLINICAL TRIALS APPROVED: 10



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Clinical trials

Following the number of requests received by the Clinical Trial Office/Pre-Authorization Area and by the GCP Inspections Office from the various stakeholders, the Italian Medicines Agency provides indications regarding the management of clinical trials in Italy during the COVID-19 (coronavirus disease 19) emergency

APPROVED CLINICAL TRIALS

- **COLVID-19 -** Randomized study on colchicine administration
- **SOLIDARITY** – WHO randomized trial
- **Hydro-Stop** - premature administration of hydroxychloroquine - ASUR-AV5 Ascoli Piceno
- **Tocilizumab 2020-001154-22 (tocilizumab)** - F. Hoffmann-La Roche Ltd
- **RCT-TCZ-COVID-19 (tocilizumab)** - AUSL – IRCSS di Reggio Emilia
- **Sarilumab COVID-19 (sarilumab)** - Sanofi-Aventis Recherche & Développement
- **Sobi.IMMUNO-101 (emapalumab/ anakinra)** - SOBI
- **TOCIVID-19 (tocilizumab)** - Istituto Nazionale Tumori, IRCSS, Fondazione G. Pascale di Napoli
- **GS-US-540-5773 (remdesivir)** - Gilead
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